

Claims

1. A polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotypic antibody or fragments thereof being capable of specifically binding an amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5.
2. An antibody according to claim 1, wherein the portion comprises the amino acid sequence of SEQ ID NO:6.
3. An antibody according to claim 1, wherein the portion comprises the amino acid sequence of SEQ ID NO:3.
4. The antibody of claim 1, wherein said antibody is an IgG antibody.
5. The antibody of claim 1, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', an F(ab')₂ and a CDR.
6. The antibody of claim 1, wherein said antibody or antibody fragment is further capable of regulating a biochemical activity of a NIK molecule.
7. The antibody according to anyone of the preceding claims, wherein said antibody or antibody fragment is further capable of specifically detecting phosphorylated NIK or a specific portion thereof.
8. The antibody according to claim 7 capable of specifically detecting phosphorylated NIK by Western immunoblotting analysis.
9. The antibody according to claim 7 capable of specifically detecting phosphorylated NIK by ELISA.
10. The antibody according to claim 7 capable of specifically detecting phosphorylated NIK by immunoprecipitation.

11. The monoclonal antibody according to claim 1, being monoclonal antibodies generated by hybridoma NIK-P4 30.12 deposited at the CNCM under No. I-3095.
12. A polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotypic antibody or fragments thereof being capable of specifically binding NIK or a mutein, functional derivative, active fraction, circularly permuted derivative or salt thereof, the antibody prepared by immunizing a mammal with an amino acid sequence, or a portion of amino acid sequence set forth in SEQ ID NO: 5.
13. An hybridoma clone deposited at the CNCM under No. I-3095
14. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as an active ingredient, a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotypic antibody or fragments thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5.
15. The pharmaceutical composition according to claim 14, wherein the amino acid portion comprises the amino acid sequence set forth in SEQ NO: 3.
16. The pharmaceutical composition according to claim 14, wherein said antibody is an IgG antibody.
17. The pharmaceutical composition according to claim 14, wherein said antibody or antibody fragment is from murine origin.
18. The pharmaceutical composition according to claim 14, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', and F(ab')₂ and a CDR.
19. The pharmaceutical composition according to claim 14, wherein said antibody is further capable of regulating a biochemical activity of a NIK molecule.
20. The pharmaceutical composition according to claim 19, for the

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inhibition of CD40 signalling.

21. The pharmaceutical composition according to claim 19, for the inhibition of CD70 signalling.
22. The pharmaceutical composition according to claim 19, for treating a disease selected from a malignant diseases and diseases associated with pathological immune responses.
23. The pharmaceutical composition according to claim 22, wherein the disease is associated with pathological immune responses selected from autoimmune, allergic, inflammatory, and transplantation-related diseases.
24. The pharmaceutical composition according to claim 23, wherein the disease is selected from, asthma, rheumatoid arthritis, inflammatory bowel disease, atherosclerosis and Alzheimer's disease.
25. The pharmaceutical composition according to claim 22, wherein the disease is a malignant disease.
26. A method of regulating a biochemical activity of a NIK molecule, the method comprising contacting the NIK molecule with a polyclonal, monoclonal, chimeric, humanized, human or anti-anti-idiotype antibody or fragments thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5, thereby regulating a biochemical activity of a NIK molecule.
27. The method according to claim 26, wherein said contacting the NIK molecule with said antibody is effected by administering said antibody to an individual.
28. The method according to claim 26, wherein said antibody is an IgG antibody.
29. The method according to claim 26, wherein said antibody or antibody fragment is of murine origin.
30. The method according to claim 26, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab',

an F(ab')₂ and a CDR.

31. A composition-of-matter comprising a substrate covalently attached to a peptide of amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 for selectively capturing the antibody or antibody fragment capable of specifically binding the target antigen.
32. The composition-of-matter according to claim 31, wherein the portion thereof comprises the amino acid sequence set forth in SEQ ID NO:3.
33. The composition-of-matter of claim 31, wherein said substrate is an affinity chromatography matrix.
34. The composition-of-matter according to claim 31, wherein said substrate comprises a carbohydrate or a derivative of said carbohydrate.
35. The composition-of-matter according to claim 31, wherein said carbohydrate is selected from the group consisting of agarose, sepharose, and cellulose.
36. The composition-of-matter according to claim 31, wherein said substrate is selected from the group consisting of a bead, a resin, or a plastic surface.
37. The use of a polyclonal, monoclonal, chimeric, humanized, human or anti-anti- idotype antibody or fragments thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 in the manufacture of a medicament for the treatment of a disease caused or aggravated by the activity of NIK.
38. The use according to claim 37, wherein said antibody is an IgG antibody.
39. The use according to claim 37, wherein said antibody or antibody fragment is derived from mouse.
40. The use according to claim 37, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab',

an F(ab')₂ and a CDR.

41. The use according to claim 37, in a disease selected from a malignant diseases and diseases associated with pathological immune responses.
42. The use according to claim 41, wherein the disease associated with pathological immune responses is selected from autoimmune, allergic, inflammatory, and transplantation-related diseases.
43. The use according to claim 42, wherein the disease is selected from, asthma, rheumatoid arthritis, inflammatory bowel disease, atherosclerosis and Alzheimer's disease.
44. The use according to claim 41, wherein the disease is a malignant disease.
45. A method for preparing a monoclonal antibody comprising growing a cloned hybridoma comprising a spleen cell from a mammal immunized with an amino acid sequence comprising SEQ ID NO: 6, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 and a homogeneous or heterogeneous lymphoid cell in liquid medium or mammalian abdomen to allow the hybridoma to produce and accumulate the monoclonal antibody.
46. A method according to claim 45, wherein the portion thereof comprises amino acid sequence set forth in SEQ ID NO: 3.
47. A method for identifying a ligand capable of inducing NIK-mediated NF κ B activation in a cell, comprising introducing an antibody or an antibody fragment according to anyone of claims 1 to 12 into a cell, incubating the cell with individual ligands, monitoring parameters indicative of NF κ B activation, and selecting the ligand by which activation of NF κ B is affected by specific blockage of NIK activity by said antibody or antibody fragment.
48. A method according to claim 47, wherein activation of NF κ B is determined by monitoring parameters indicative of the canonical pathway activation of NF κ B.
49. A method according to claim 48, wherein activation of NF κ B is

determined by monitoring I κ B α degradation.

50. A method according to claim 49, wherein the cells are of lymphoblastoid type.
51. A method according to claim 50, wherein the cells are selected from Ramos, BJAB, and Jurkat cells.
52. A method of treatment of a disease caused or aggravated by the activity of NIK, comprises the administration of a polyclonal, monoclonal, chimeric, humanized, human or anti-anti- idotype antibody or fragments thereof being capable of specifically binding the amino acid sequence set forth in SEQ ID NO: 5, or a portion thereof wherein the amino acid sequence or portion thereof comprises a phosphorylated threonine at amino acid position 559 of SEQ ID NO: 5 to an individual in need.
53. The method according to claim 52, wherein said antibody is an IgG antibody.
54. The method according to claim 52, wherein said antibody or antibody fragment is derived from mouse.
55. The method according to claim 52, wherein said antibody fragment is selected from the group consisting of a single-chain Fv, an Fab, an Fab', an F(ab')₂ and a CDR.
56. A method of treatment according to claim 52, wherein the disease is selected from a malignant diseases and diseases associated with pathological immune responses.
57. A method of treatment according to claim 56, wherein the disease associated with pathological immune responses is selected from autoimmune, allergic, inflammatory, and transplantation-related diseases.
58. A method of treatment according to claim 57, wherein the disease is selected from, asthma, rheumatoid arthritis, inflammatory bowel disease, atherosclerosis and Alzheimer's disease.
59. A method of treatment according to claim 56, wherein the disease is a

malignant disease.

60. A method for the purification of a NIK binding protein, which comprises contacting a sample containing NIK and the NIK-binding protein with an antibody according to anyone of claims 1 to 12, co-immunoprecipitating the NIK and NIK-binding protein, washing the immune complex produced, and recovering the NIK-binding protein from the immune complex using a competing peptide derived from NIK.
61. A method according to claim 60, wherein the sample is selected from body fluids, cell extracts and DNA expression libraries.
62. The use of an antibody according to anyone of claims 1 to 12 for the development of an ELISA assay.
63. The use an antibody according to anyone of claims 1 to 12, for the immune purification of NIK or a mutein, functional derivative, active fraction, circularly permuted derivative or salt thereof.